



USSN 09/782,855.

Case 20526Y

Page 2

RECEIVED

JUL 08 2002

REMARKS

TECH CENTER 1600/2900

Claims 1-21 are pending in the instant application. Claims 1-21 have been rejected.

Rejection of Claims 1-21 under 35 USC §112, first paragraph

The Examiner has rejected Claims 1-21 under 35 USC §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, the Examiner stated that:

Claims 1-21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for non-heterocyclic, does not reasonably provide enablement for example, [N, O and S containing heterocyclic] derivatives. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims. There is insufficient enabling disclosure to support the terms heteroaryl and hetero arylalkyl in R₃, R₁₀ and 9 [sic].

The specification does not give any guidance as to how each of the heterocyclic substituted derivatives were prepared. In In re Wands, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 25 U.S.C. §112, first paragraph, have been described. They are: 1. nature of the invention, 2. the state of the prior art, 3. the predictability or lack thereof in the art, 4. the amount of direction or guidance present, 5. The presence or absence of working examples, 6. the breadth of the claims, 7. the quantity of experimentation needed, and 8. the level of skill in the art.

In the instant case, Applicants are claiming heterocyclic substituted tetrahydrofluorenone derivatives. Applicants have not disclosed any working examples which would demonstrate, or guide, one skilled in the art as to the heterocyclic substituted derivatives other than 5 and 6 member mono ring, N-heterocyclic derivatives, were prepared or obtained. The process of making the heterocyclic substituted derivatives or how the heterocyclic substituted derivatives were obtained is not readily apparent from the specification.

The specification must teach how to make the invention. In re Gardner, 166 U.S.P.Q. 138 (1970). In order to practice the claimed invention, one skilled in the art would have to speculate how the heterocycle containing derivatives were obtained or prepared. Therefore, the instant invention is not enabled. Claims limiting the scope of these terms should overcome this rejection.

Applicants respectfully traverse this rejection. Applicants assert that the specification does enable the claims and provides ample guidance as to how heterocyclic and heteroaryl substituted derivatives are prepared.

In order to make a rejection based upon lack of enablement, *the Examiner has the initial burden* to establish a reasonable basis to question the enablement provided for the claimed invention (MPEP §2164.04). “A specification disclosure which contains a teaching...must be taken as being in compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, *unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support*” (MPEP 2164.04, emphasis added). The Examiner has not met the initial burden of establishing a reasonable basis to question the enablement provided in the specification.

Even if the initial burden required had been met, the Examiner has not presented sufficient evidence that the claims are not enabled by the disclosure. Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. §112, first paragraph, have been described, *see In re Wands*, 8 USPQ2d 1400 (1988) and the Examiner’s argument, *supra*.

The MPEP explains that “the Examiner’s analysis must consider all the evidence related to each of these factors, and any conclusion of nonenablement must be based on the evidence as a whole” (MPEP § 2164.01(a)).

As the nature of the invention is in the chemical arts, there is limited predictability in the field. However, “the scope of the required enablement varies inversely with the degree of predictability involved, but even in unpredictable arts, a disclosure of every operable species is not required” (MPEP § 2164.03, emphasis added). Applicants have provided sufficient direction and guidance to one skilled in the art wishing to make the compounds of the present invention, and have included 117 pages of extensive experimental direction that includes over 100 working examples. In addition, the prior art is rich with disclosure about tetrahydrofluorenone synthesis. Accordingly, based upon the disclosure in the specification along with the teachings in the prior art, one skilled in the art would not have to undergo undue experimentation to arrive at the compounds of the present invention.

One skilled in the art, after reading the instant specification and relevant prior art, could successfully attach a heteroaryl or heteroarylalkyl substituent at the R³ position. In fact, the specification provides working examples depicting R³ as heteroaryl groups, for instance in Example 9 on page 53 (thiophenyl at R³ position) and Example 27 on page 115 (furanyl at R³ position).

Also, after reading the instant specification and relevant prior art, one skilled in the art could attach a heteroaryl or heteroarylalkyl substituent at the R¹⁰ position. The specification provide examples of methyl-cyclohexyl and methyl-cyclopentyl substituents at the R¹⁰ position. Given the extensive experimental direction provided in the specification, a heteroaryl or heteroarylalkyl derivative can be synthesized by analogy.

The Examiner contends that “there is insufficient enabling disclosure to support the terms heteroaryl and hetero arylalkyl in R₃, R₁₀ and 9.” Applicants are assuming that the Examiner meant “R⁹” instead of “9.” Applicants traverse this rejection as R⁹ is not defined as heteroaryl or heteroarylalkyl; R⁹ is defined as being selected from the group consisting of hydrogen, C₁-6alkyl, C₂-6alkenyl, and C₂-6alkynyl, or R⁸ and R⁹, when taken together with the carbon atom to which they are attached, form a 3-5 membered cycloalkyl ring.



USSN 09/782,855
Case 20526Y
Page 5

The Examiner has not made a prima facie case of nonenablement, and in light of the arguments presented, it is not reasonable to conclude that Applicant has not enabled the claims. Accordingly, Applicants respectfully request the rejection of claims 1-21 under 35 USC §112, first paragraph, be withdrawn. Applicants maintain that the application is in condition for allowance and passage to issue is earnestly requested.

If a telephonic communication with the Applicants' representative will advance the prosecution of the instant application, please telephone the representative indicated below. Applicants believe no additional fees are due but the Commissioner is authorized to charge any fees required in connection with this response to Merck Deposit Account No. 13-2755.

Respectfully submitted,

By Nicole M. Wallinger

Nicole M. Wallinger

Reg. No. 45,194

Attorney for Applicants

MERCK & CO., INC.

P.O. Box 2000

Rahway, New Jersey 07065-0907

(732) 594-1077

Date: June 25, 2002

TECH CENTER 1600/2900

JUL 08 2002

RECEIVED